1: NM_075774. Caenorhabditis el...[gi:25150522] Links

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LOCUS       NM_075774               1473 bp    mRNA    linear   INV 12-JUL-2003
DEFINITION  Caenorhabditis elegans  Suppressor/Enhancer of Lin-12 SEL-12,
            SUppressor of Multi-vulva phenotype SUM-1, presenilin, membrane
            protein facilitator of Notch receptors signaling (50.0 kD) (sel-12)
            complete mRNA.
ACCESSION   NM_075774
VERSION     NM_075774.2  GI:25150522
KEYWORDS    .
SOURCE      Caenorhabditis elegans (worm)
  ORGANISM  Caenorhabditis elegans
            Eukaryota ; Metazoa ; Nematoda ; Chromadorea ; Rhabditida ;
            Rhabditoidea ; Rhabditidae ; Peloderinae ; Caenorhabditis.
REFERENCE   1  (bases 1 to 1473)
  AUTHORS   Lakowski,B., Eimer,S., Gobel,C., Bottcher,A., Wagler,B. and
            Baumeister,R.
  TITLE     Two suppressors of sel-12 encode C2H2 zinc-finger proteins that
            regulate presenilin transcription in Caenorhabditis elegans
  JOURNAL   Development 130 (10), 2117-2128 (2003)
  MEDLINE   22554535
   PUBMED   12668626
REFERENCE   2  (bases 1 to 1473)
  AUTHORS   Kitagawa,N., Shimohama,S., Oeda,T., Uemura,K., Kohno,R., Kuzuya,A.,
            Shibasaki,H. and Ishii,N.
  TITLE     The role of the presenilin-1 homologue gene sel-12 of
            Caenorhabditis elegans in apoptotic activities
  JOURNAL   J. Biol. Chem. 278 (14), 12130-12134 (2003)
  MEDLINE   22552452
   PUBMED   12556527
REFERENCE   3  (bases 1 to 1473)
  AUTHORS   Eimer,S., Donhauser,R. and Baumeister,R.
  TITLE     The Caenorhabditis elegans presenilin sel-12 is required for
            mesodermal patterning and muscle function
  JOURNAL   Dev. Biol. 251 (1), 178-192 (2002)
  MEDLINE   22301592
   PUBMED   12413907
REFERENCE   4  (bases 1 to 1473)
  AUTHORS   Eimer,S., Lakowski,B., Donhauser,R. and Baumeister,R.
  TITLE     Loss of spr-5 bypasses the requirement for the C.elegans presenilin
            sel-12 by derepressing hop-1
  JOURNAL   EMBO J. 21 (21), 5787-5796 (2002)
  MEDLINE   22299931
   PUBMED   12411496
REFERENCE   5  (bases 1 to 1473)
  AUTHORS   Li,J., Pauley,A.M., Myers,R.L., Shuang,R., Brashler,J.R., Yan,R.,
            Buhl,A.E., Ruble,C. and Gurney,M.E.
  TITLE     SEL-10 interacts with presenilin 1, facilitates its ubiquitination,
            and alters A-beta peptide production
  JOURNAL   J. Neurochem. 82 (6), 1540-1548 (2002)
  MEDLINE   22242246
   PUBMED   12354302
REFERENCE   6  (bases 1 to 1473)
  AUTHORS   Francis,R., McGrath,G., Zhang,J., Ruddy,D.A., Sym,M., Apfeld,J.,
            Nicoll,M., Maxwell,M., Hai,B., Ellis,M.C., Parks,A.L., Xu,W.,
            Li,J., Gurney,M., Myers,R.L., Himes,C.S., Hiebsch,R., Ruble,C.,
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Nye,J.S. and Curtis,D.
TITLE aph-1 and pen-2 are required for Notch pathway signaling, gamma-secretase cleavage of betaAPP, and presenilin protein accumulation
JOURNAL Dev. Cell 3 (1), 85-97 (2002)
MEDLINE 22105644
PUBMED 12110170
REFERENCE 7 (bases 1 to 1473)
AUTHORS Levitan,D., Yu,G., St George Hyslop,P. and Goutte,C.
TITLE APH-2/nicastrin functions in LIN-12/Notch signaling in the Caenorhabditis elegans somatic gonad
JOURNAL Dev. Biol. 240 (2), 654-661 (2001)
MEDLINE 21643937
PUBMED 11784090
REFERENCE 8 (bases 1 to 1473)
AUTHORS Maruyama,S., Hatakeyama,S., Nakayama,K., Ishida,N., Kawakami,K. and Nakayama,K.
TITLE Characterization of a mouse gene (Fbxw6) that encodes a homologue of Caenorhabditis elegans SEL-10
JOURNAL Genomics 78 (3), 214-222 (2001)
MEDLINE 21601157
PUBMED 11735228
REFERENCE 9 (bases 1 to 1473)
AUTHORS Cinar,H.N., Sweet,K.L., Hosemann,K.E., Earley,K. and Newman,A.P.
TITLE The SEL-12 presenilin mediates induction of the Caenorhabditis elegans uterine pi cell fate
JOURNAL Dev. Biol. 237 (1), 173-182 (2001)
MEDLINE 21409869
PUBMED 11518514
REFERENCE 10 (bases 1 to 1473)
AUTHORS Okochi,M., Eimer,S., Bottcher,A., Baumeister,R., Romig,H., Walter,J., Capell,A., Steiner,H. and Haass,C.
TITLE A loss of function mutant of the presenilin homologue SEL-12 undergoes aberrant endoproteolysis in Caenorhabditis elegans and increases abeta 42 generation in human cells
JOURNAL J. Biol. Chem. 275 (52), 40925-40932 (2000)
MEDLINE 20576248
PUBMED 11013240
REFERENCE 11 (bases 1 to 1473)
AUTHORS Wen,C., Levitan,D., Li,X. and Greenwald,I.
TITLE spr-2, a suppressor of the egg-laying defect caused by loss of sel-12 presenilin in Caenorhabditis elegans, is a member of the SET protein subfamily
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 97 (26), 14524-14529 (2000)
MEDLINE 20570513
PUBMED 11114162
REFERENCE 12 (bases 1 to 1473)
AUTHORS Zhang,D.M., Levitan,D., Yu,G., Nishimura,M., Chen,F., Tandon,A., Kawarai,T., Arawaka,S., Supala,A., Song,Y.Q., Rogaeva,E., Liang,Y., Holmes,E., Milman,P., Sato,C., Zhang,L. and St George-Hyslop,P.
TITLE Mutation of the conserved N-terminal cysteine (Cys92) of human presenilin 1 causes increased A beta42 secretion in mammalian cells but impaired Notch/lin-12 signalling in C. elegans
JOURNAL Neuroreport 11 (14), 3227-3230 (2000)
MEDLINE 20496269
PUBMED 11043553
REFERENCE 13 (bases 1 to 1473)
AUTHORS Yu,G., Nishimura,M., Arawaka,S., Levitan,D., Zhang,L., Tandon,A., Song,Y.Q., Rogaeva,E., Chen,F., Kawarai,T., Supala,A., Levesque,L., Yu,H., Yang,D.S., Holmes,E., Milman,P., Liang,Y., Zhang,D.M., Xu,D.H., Sato,C., Rogaev,E., Smith,M., Janus,C., Zhang,Y., Aebersold,R., Farrer,L.S., Sorbi,S., Bruni,A., Fraser,P. and St George-Hyslop,P.
TITLE Nicastrin modulates presenilin-mediated notch/glp-1 signal transduction and betaAPP processing
JOURNAL Nature 407 (6800), 48-54 (2000)
MEDLINE 20445163

PUBMED 10993067
REFERENCE 14 (bases 1 to 1473)
AUTHORS Wittenburg,N., Eimer,S., Lakowski,B., Rohrig,S., Rudolph,C. and Baumeister,R.
TITLE Presenilin is required for proper morphology and function of neurons in C. elegans
JOURNAL Nature 406 (6793), 306-309 (2000)
MEDLINE 20372200
PUBMED 10917532
REFERENCE 15 (bases 1 to 1473)
AUTHORS Jacobsen,H., Reinhardt,D., Brockhaus,M., Bur,D., Kocyba,C., Kurt,H., Grim,M.G., Baumeister,R. and Loetscher,H.
TITLE The influence of endoproteolytic processing of familial Alzheimer's disease presenilin 2 on abeta42 amyloid peptide formation
JOURNAL J. Biol. Chem. 274 (49), 35233-35239 (1999)
MEDLINE 20044792
PUBMED 10575009
REFERENCE 16 (bases 1 to 1473)
AUTHORS Berezovska,O., Frosch,M., McLean,P., Knowles,R., Koo,E., Kang,D., Shen,J., Lu,F.M., Lux,S.E., Tonegawa,S. and Hyman,B.T.
TITLE The Alzheimer-related gene presenilin 1 facilitates notch 1 in primary mammalian neurons
JOURNAL Brain Res. Mol. Brain Res. 69 (2), 273-280 (1999)
MEDLINE 99296661
PUBMED 10366748
REFERENCE 17 (bases 1 to 1473)
AUTHORS Ray,W.J., Yao,M., Nowotny,P., Mumm,J., Zhang,W., Wu,J.Y., Kopan,R. and Goate,A.M.
TITLE Evidence for a physical interaction between presenilin and Notch
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 96 (6), 3263-3268 (1999)
MEDLINE 99179050
PUBMED 10077672
REFERENCE 18 (bases 1 to 1473)
AUTHORS Westlund,B., Parry,D., Clover,R., Basson,M. and Johnson,C.D.
TITLE Reverse genetic analysis of Caenorhabditis elegans presenilins reveals redundant but unequal roles for sel-12 and hop-1 in Notch-pathway signaling
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 96 (5), 2497-2502 (1999)
MEDLINE 99162634
PUBMED 10051671
REFERENCE 19 (bases 1 to 1473)
AUTHORS Hong,C.S., Caromile,L., Nomata,Y., Mori,H., Bredesen,D.E. and Koo,E.H.
TITLE Contrasting role of presenilin-1 and presenilin-2 in neuronal differentiation in vitro
JOURNAL J. Neurosci. 19 (2), 637-643 (1999)
MEDLINE 99098950
PUBMED 9880584
REFERENCE 20 (bases 1 to 1473)
AUTHORS Wu,G., Hubbard,E.J., Kitajewski,J.K. and Greenwald,I.
TITLE Evidence for functional and physical association between Caenorhabditis elegans SEL-10, a Cdc4p-related protein, and SEL-12 presenilin
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 95 (26), 15787-15791 (1998)
MEDLINE 99080092
PUBMED 9861048
REFERENCE 21 (bases 1 to 1473)
AUTHORS Levitan,D. and Greenwald,I.
TITLE Effects of SEL-12 presenilin on LIN-12 localization and function in Caenorhabditis elegans
JOURNAL Development 125 (18), 3599-3606 (1998)
MEDLINE 98384316
PUBMED 9716525
REFERENCE 22 (bases 1 to 1473)
AUTHORS Berezovska,O., Xia,M.Q. and Hyman,B.T.
TITLE Notch is expressed in adult brain, is coexpressed with presenilin-1, and is altered in Alzheimer disease

JOURNAL J. Neuropathol. Exp. Neurol. 57 (8), 738-745 (1998)
MEDLINE 98385443
PUBMED 9720489
REFERENCE 23 (bases 1 to 1473)
AUTHORS Li,X. and Greenwald,I.
TITLE Additional evidence for an eight-transmembrane-domain topology for Caenorhabditis elegans and human presenilins
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 95 (12), 7109-7114 (1998)
MEDLINE 98284066
PUBMED 9618547
REFERENCE 24 (bases 1 to 1473)
AUTHORS Davis,J.A., Naruse,S., Chen,H., Eckman,C., Younkin,S., Price,D.L., Borchelt,D.R., Sisodia,S.S. and Wong,P.C.
TITLE An Alzheimer's disease-linked PS1 variant rescues the developmental abnormalities of PS1-deficient embryos
JOURNAL Neuron 20 (3), 603-609 (1998)
MEDLINE 98198534
PUBMED 9539132
REFERENCE 25 (bases 1 to 1473)
AUTHORS Zhang,W., Han,S.W., McKeel,D.W., Goate,A. and Wu,J.Y.
TITLE Interaction of presenilins with the filamin family of actin-binding proteins
JOURNAL J. Neurosci. 18 (3), 914-922 (1998)
MEDLINE 98099802
PUBMED 9437013
REFERENCE 26 (bases 1 to 1473)
AUTHORS Mattson,M.P., Guo,Q., Furukawa,K. and Pedersen,W.A.
TITLE Presenilins, the endoplasmic reticulum, and neuronal apoptosis in Alzheimer's disease
JOURNAL J. Neurochem. 70 (1), 1-14 (1998)
MEDLINE 98082804
PUBMED 9422341
REFERENCE 27 (bases 1 to 1473)
AUTHORS Mattson,M.P. and Guo,Q.
TITLE Cell and molecular neurobiology of presenilins: a role for the endoplasmic reticulum in the pathogenesis of Alzheimer's disease?
JOURNAL J. Neurosci. Res. 50 (4), 505-513 (1997)
MEDLINE 98067216
PUBMED 9404712
REFERENCE 28 (bases 1 to 1473)
AUTHORS Li,X. and Greenwald,I.
TITLE HOP-1, a Caenorhabditis elegans presenilin, appears to be functionally redundant with SEL-12 presenilin and to facilitate LIN-12 and GLP-1 signaling
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 94 (22), 12204-12209 (1997)
MEDLINE 98004548
PUBMED 9342387
REFERENCE 29 (bases 1 to 1473)
AUTHORS Hutton,M. and Hardy,J.
TITLE The presenilins and Alzheimer's disease
JOURNAL Hum. Mol. Genet. 6 (10), 1639-1646 (1997)
MEDLINE 97444123
PUBMED 9300655
REFERENCE 30 (bases 1 to 1473)
AUTHORS Wong,P.C., Zheng,H., Chen,H., Becher,M.W., Sirinathsinghji,D.J., Trumbauer,M.E., Chen,H.Y., Price,D.L., Van der Ploeg,L.H. and Sisodia,S.S.
TITLE Presenilin 1 is required for Notch1 and DII1 expression in the paraxial mesoderm
JOURNAL Nature 387 (6630), 288-292 (1997)
MEDLINE 97297761
PUBMED 9153393
REFERENCE 31 (bases 1 to 1473)
AUTHORS Baumeister,R., Leimer,U., Zweckbronner,I., Jakubek,C., Grunberg,J. and Haass,C.
TITLE Human presenilin-1, but not familial Alzheimer's disease (FAD) mutants, facilitate Caenorhabditis elegans Notch signalling

independently of proteolytic processing
JOURNAL Genes Funct. 1 (2), 149-159 (1997)
MEDLINE 98343909
PUBMED 9680315
REFERENCE 32 (bases 1 to 1473)
AUTHORS Hong,C.S. and Koo,E.H.
TITLE Isolation and characterization of Drosophila presenilin homolog
JOURNAL Neuroreport 8 (3), 665-668 (1997)
MEDLINE 97260623
PUBMED 9106743
REFERENCE 33 (bases 1 to 1473)
AUTHORS Berezovska,O., Xia,M.Q., Page,K., Wasco,W., Tanzi,R.E. and Hyman,B.T.
TITLE Developmental regulation of presenilin mRNA expression parallels notch expression
JOURNAL J. Neuropathol. Exp. Neurol. 56 (1), 40-44 (1997)
MEDLINE 97144360
PUBMED 8990127
REFERENCE 34 (bases 1 to 1473)
AUTHORS Levitan,D., Doyle,T.G., Brousseau,D., Lee,M.K., Thinakaran,G., Slunt,H.H., Sisodia,S.S. and Greenwald,I.
TITLE Assessment of normal and mutant human presenilin function in Caenorhabditis elegans
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 93 (25), 14940-14944 (1996)
MEDLINE 97121494
PUBMED 8962160
REFERENCE 35 (bases 1 to 1473)
AUTHORS Li,X. and Greenwald,I.
TITLE Membrane topology of the C. elegans SEL-12 presenilin
JOURNAL Neuron 17 (5), 1015-1021 (1996)
MEDLINE 97092712
PUBMED 8938132
REFERENCE 36 (bases 1 to 1473)
AUTHORS Levitan,D. and Greenwald,I.
TITLE Facilitation of lin-12-mediated signalling by sel-12, a Caenorhabditis elegans S182 Alzheimer's disease gene
JOURNAL Nature 377 (6547), 351-354 (1995)
MEDLINE 96032531
PUBMED 7566091
COMMENT REVIEWED REFSEQ: This record has been curated by NCBI staff. The reference sequence was derived from U35660 and AV179958.1.
On Nov 21, 2002 this sequence version replaced gi:17569442.
Summary: This gene sel-12, also known as sum-1, F35H12.3, XB535 or YK4554, maps at (X; -19.01). Its phenotype is suppressor/enhancer of lin-12, suppressor of multi-vulva phenotype, facilitator of notch-type receptors signaling. It encodes a presenilin, membrane protein facilitator of Notch receptors signaling. From Pfam homology, the product would be involved in intracellular signaling cascade and would localize in membrane.

According to the Worm Transcriptome Project, it is well expressed in L3, L4, adult and culminating in embryos [Kohara cDNAs]. Its sequence is defined by 11 cDNA clones.

Phenotype
[from C. elegans II book] Allele ar131: (previously known as sum-1) recessive suppressor of multivulva phenotype of lin-12 hypermorph n950; impenetrant egg laying defective in lin-12 (+) background. Three other alleles: ar133, ar171 (100% egg laying defective, ar171/Df similar, W225opal). Cloned: encodes predicted 467 aa protein, 9 transmembrane domains; related to human presenilin genes (S182) and to SPE-4. [Levitan and Greenwald 1995; Iva Greenwald].
Allele ar131, ar40.
[Levitan D] suppressor of multivulva phenotype.
Selected strains available from the CGC.
GS883 dpy-5(e61) sel(ar40)I; unc-32(e189) lin-12(n676n930)III

[Greenwald IS] DpyUnc. ar40 is a semi-dominant suppressor. At 25C ar40 suppresses the Egl phenotype of ne676n930. At 15C a high percentage of hermaphrodites have a 0 AC-Egl phenotype. ar40 suppresses proximal mitosis. ar40 does not suppress vulval lineage defects.
AN87 sel-12(ty11) X [Anna Newman, Nese Cinar, EMS] Egl. Premature stop codon.

RNA interference results:
[J.Ahringer 2003] No obvious phenotype (by feeding genomic PCR product JA:F35H12.3). Warning: this double stranded RNA may also interfere with gene XB537.

Function
Protein properties: [GB:AF171064] function: facilitator of Notch receptors signaling.
membrane protein similar to Homo sapiens PS1 andPS2.
[WormBase] The sel-12 gene encodes a ortholog of human PS1, which when mutated leads to type 3 Alzheimer disease (OMIM:104311); it is also homologous to PS2, which when mutated leads type 4 Alzheimer disease (OMIM:600759).

Expression
The expression profile for the gene, derived from the proportion of animals at each stage in each Kohara library is: embryos 76%, L1 or L2 larvae 1%, L3 to adult 22%.
In situ hybridisation pictures to all stages of development are available from Kohara NextDB.
For a detailed expression pattern description, see Wormbase Expr1288, Expr1609.

Interactions
This gene interacts with:
gene spr-1: spr-1 loss of function suppresses Egl of sel-12.
protein LIN-12.
protein SEL-10CO.

This complete mRNA is 1473 bp long. Its sequence exactly matches the genome. The premessenger has 7 exons. It covers 2.42 kb on the WS97 genome. It is transpliced to SL1. The protein (444 aa, 50.0 kDa, pI 6.7) contains one Presenilin motif. It also contains at least 8 transmembrane domain, a prenylation domain, an ER membrane domain [Psort2]. It is predicted to localise in the plasma membrane [Psort2]. Taxblast (threshold 10^-3) tracks ancestors down to eukaryota.
COMPLETENESS: full length.

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                     /locus_tag="XB535"
                     /note="Exon 6 length 207 bp"
     misc_feature    bond(1066,1067)
                     /gene="sel-12"
                     /locus_tag="XB535"
                     /note="Intron length 422 bp, type gt_ag"
     exon            1067..1473
                     /gene="sel-12"
                     /locus_tag="XB535"
                     /note="Exon 7 length 407 bp"
     3'UTR           1336..1473
                     /gene="sel-12"
                     /locus_tag="XB535"
                     /note="The 3' UTR contains 138 bp followed by the polyA.
                     The standard AATAAA polyadenylation signal does not occur,
                     but the variant ATTAAA is seen about 15 bp before the
                     polyA."
                     /evidence=experimental
     polyA_signal    1459..1464
                     /gene="sel-12"
                     /locus_tag="XB535"
                     /note="variant  attaaa"
     polyA_site      1473
                     /gene="sel-12"
                     /locus_tag="XB535"
                     /note="PolyA visible in U35660, yk452b9"
                     /evidence=experimental
BASE COUNT      381 a    313 c    312 g    467 t
ORIGIN
        1 atgccttcca caaggagaca acaggagggc ggaggtgcag atgcggaaac acataccgtt
       61 tacggtacaa atctgataac aaatcggaat agccaagaag acgaaaatgt tgtggaagaa
      121 gcggagctga aatacggagc atctcacgtt attcatctat ttgtgccggt gtcactatgc
      181 atggctctgg ttgtttttac gatgaacacg attacgtttt atagtcaaaa caatggaagg
      241 catttactat acactccttt tgtccgggaa acagacagta tcgttgagaa gggattgatg
      301 tcacttggaa atgctctcgt catgttgtgc gtggtcgttc tgatgacagt tctgctgatt
      361 gttttctata aatacaagtt ttataagctt attcatggat ggcttattgt cagcagtttt
      421 cttcttcttt tcctattcac tacaatctat gtgcaagaag ttctgaaaag tttcgatgtg
      481 tctcccagcg cactattggt tttgtttgga ctgggtaact atggagttct cggaatgatg
      541 tgtatacatt ggaaaggtcc attgcgtctg caacagttct accttattac aatgtctgca
      601 ctaatggctc tggtctttat caagtaccta ccagaatgga ctgtgtggtt tgtgctgttt
      661 gttatctcgg tttgggatct ggttgccgtg ctcacaccaa aaggaccatt gagatatttg
      721 gtggaaactg cacaggagag aaacgagcca attttcccgg cgctgattta ttcgtctgga
      781 gtcatctatc cctacgttct tgttactgca gttgaaaaca cgacagaccc ccgtgaaccg
      841 acgtcgtcag actcaaatac ttctacagct tttcctggag aggcgagttg ttcatctgaa
      901 acgccaaaac ggccaaaagt gaaacgaatt cctcaaaaag tgcaaatcga atcgaatact
      961 acagcttcaa cgacacaaaa ctctggagta agggtggaac gggagctagc tgctgagaga
     1021 ccaactgtac aagacgccaa ttttcacagg cacgaagagg aagagagagg tgtgaaactt
     1081 ggtctgggcg acttcatttt ctactctgtt ctcctcggca aggcttcatc gtactttgac
     1141 tggaacacga ctatcgcttg ttatgtggcc attcttatcg gtctctgctt cactcttgtc
     1201 ctgctcgccg tcttcaaacg agcactcccg gctctgccaa tttccatttt ctccggactc
     1261 atttttact tttgtacccg ctggatcatc accccatttg ttacacaagt ctctcaaaag
     1321 tgtttattat attaattctc tgtttttgcc atttctttgc atcatcaact tttcgattat
     1381 atcttgagcg atctcaaagc tttattttac atacctattt atttttgaac tttgtcattt
     1441 aagttatata aataatttat taaacgtttc tgc
//
```